## CLAIMS

1. An isolated polypeptide having the ability to bind fibrin comprising the amino acid sequence Tyr–Tyr–Gly–Xaa, wherein Xaa is selected from Thr, Ser or Val.

2. An isolated polypeptide comprising the amino acid sequence Cys–$X_2$–$X_3$–Tyr–$X_5$–$X_6$–Cys (SEQ ID NO: 2), wherein

   $X_2$ is Ala, Glu, Phe, Gly, Ile, Lys, Leu, Met, Arg, Thr, Val, Tyr, Asn, Asp, Gln, His, Ser, or Trp;

   $X_3$ is Ser, Phe, Ala, or Tyr;

   $X_5$ is Gly, Ala, or DAla; and

   $X_6$ is Thr, Val, or Ser.

3. A polypeptide according to Claim 2 wherein the amino acid residue $X_5$ is Gly and the amino acid residue $X_6$ is Thr.

4. An isolated polypeptide comprising the amino acid sequence $X_1$–$X_2$–Cys–$X_4$–$X_5$–Tyr–$X_7$–$X_8$–Cys–$X_{10}$–$X_{11}$ (SEQ ID NO:1), wherein

   $X_1$ is Arg, Asp, His, Leu, or Phe;

   $X_2$ is Ala, Asp, Gly, Pro, or Ser;

   $X_4$ is Ala, Glu, Phe, Gly, Ile, Lys, Leu, Met, Arg, Thr, Val, Tyr, Asn, Asp, Gln, His, Ser, or Trp;

   $X_5$ is Ala, Tyr, Phe, or Ser;

   $X_7$ is Gly, Ala, or DAla;

   $X_8$ is Thr, Val, or Ser;

   $X_{10}$ is His, Leu, or Phe;

   $X_{11}$ is Arg, Asp, or His.

5. An isolated polypeptide comprising the amino acid sequence
Cys–Tyr–$X_3$–Ser–Tyr–$X_6$–$X_7$–$X_8$–$X_9$–Cys (SEQ ID NO: 17), wherein
$X_3$ is Asn or Asp;
$X_6$ is Gly or Tyr;
$X_7$ is His or Val;
$X_8$ is Pro or Trp; and
$X_9$ is Trp or Tyr.

6. An isolated polypeptide comprising the amino acid sequence
$X_1$–$X_2$–$X_3$–Cys–Tyr–$X_6$–Ser–Tyr–$X_9$–$X_{10}$–$X_{11}$–$X_{12}$–Cys–$X_{14}$–$X_{15}$–$X_{16}$ (SEQ ID NO: 65), wherein
$X_1$ is Asn or Arg;
$X_2$ is His or Phe;
$X_3$ is Gly or Leu;
$X_6$ is Asn or Asp;
$X_9$ is Gly or Tyr;
$X_{10}$ is Val or His;
$X_{11}$ is Pro or Trp;
$X_{12}$ is Tyr or Trp;
$X_{14}$ is Asp or Ser;
$X_{15}$ is Tyr or His; and
$X_{16}$ is Ser or His.

7. An isolated polypeptide comprising the amino acid sequence Cys–Pro–Tyr–Xaa–Leu–Cys (SEQ ID NO: 20), where Xaa is Asp or Gly.

8. An isolated polypeptide comprising the amino acid sequence $X_1$–$X_2$–Cys–Pro–Tyr–$X_6$–Leu–Cys–$X_9$–$X_{10}$–$X_{11}$ (SEQ ID NO: 66), wherein
$X_1$ is Trp, Phe, His, or Tyr;
$X_2$ is His, Asp, or Glu;

$X_6$ is Asp, Gly, or Ala;

$X_9$ is His, Phe, Tyr, or Trp;

$X_{10}$ is Ile, Leu, or Val; and

$X_{11}$ is Asn, Gln, Ile, Leu, or Val.

9. An isolated polypeptide comprising an amino acid sequence selected from the group consisting of:

Arg–Ser–Cys–Asn–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:5);

His–Asp–Cys–Gln–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:6);

Phe–Ala–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:7);

Arg–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Phe–Asp (SEQ ID NO:8);

Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO:9);

Phe–Ser–Cys–Trp–Tyr–Ser–Leu–His–Cys–His–Arg (SEQ ID NO:10);

Asp–Pro–Cys–Ser–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:11);

Leu–Pro–Cys–Ser–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:12);

Leu–Ser–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Arg (SEQ ID NO:13);

Leu–Ala–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:14);

Asp–Gly–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:15);

Arg–Pro–Cys–Asn–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:16)

Asn–His–Gly–Cys–Tyr–Asn–Ser–Tyr–Gly–Val–Pro–Tyr–Cys–Asp–Tyr–Ser (SEQ ID NO: 18);

Arg–Phe–Leu–Cys–Tyr–Asp–Ser–Tyr–Tyr–His–Trp–Trp–Cys–Ser–His–His (SEQ ID NO: 19);

Trp–Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 21),

Gln–Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 22),

Gly–Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 23),

Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 24),

His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 25),

Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile (SEQ ID NO: 26),

Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 27),

Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 28),

Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile (SEQ ID NO: 29),

Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu (SEQ ID NO: 32),

Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu (SEQ ID NO: 33),

Cys–Asp–Tyr–Tyr–Gly–Thr–Cys (SEQ ID NO: 34),

Asp–Tyr–Tyr–Gly–Thr (SEQ ID NO: 35),

Leu–Pro–Cys–Asp–Tyr–Tyr–DAla–Thr–Cys–Leu–Asp (SEQ ID NO: 40),

Leu–Ala–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO: 41),

Leu–Pro–Cys–Ala–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO: 42),

Leu–Pro–Cys–Asp–Ala–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO: 43),

Leu–Pro–Cys–Asp–Tyr–Ala–Gly–Thr–Cys–Leu–Asp (SEQ ID NO: 44),

Leu–Pro–Cys–Asp–Tyr–Tyr–Ala–Thr–Cys–Leu–Asp (SEQ ID NO: 45),

Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Ala–Cys–Leu–Asp (SEQ ID NO: 46),

Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Ala–Asp (SEQ ID NO: 47),

Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Ser–Cys–Leu–Asp (SEQ ID NO: 48),

Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Val–Cys–Ala–Asp (SEQ ID NO: 51),

Gly–Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 57),

Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 58),

His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 59),

Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile (SEQ ID NO: 60),

Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 61),

Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 62), and

Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile (SEQ ID NO: 63).

10. A polypeptide according to any one of Claims 2 – 9, wherein said polypeptide selectively binds fibrin and not fibrinogen.

11. A polypeptide according to Claim 10, wherein said polypeptide has a $K_d$ for fibrinogen which is at least about 1.5 times greater than its $K_d$ for fibrin.

12. A polypeptide according to Claim 11, wherein said polypeptide has a $K_d$ for fibrinogen which is at least about 10 times greater than its $K_d$ for fibrin.

13. A polypeptide according to Claim 12, wherein said polypeptide has a $K_d$ for fibrinogen which is at least about 100 times greater than its $K_d$ for fibrin.

14. A polypeptide according to Claim 13, wherein said polypeptide has a $K_d$ for fibrinogen which is at least about 1000 times greater than its $K_d$ for fibrin.

15. A cyclic compound having the formula selected from the group consisting of (I), (II), (III) and (IV) as depicted in Table 12.

16. A method for isolating phage that bind fibrin or a fibrin–derived protein but not fibrinogen, comprising the steps of:

a) immobilizing fibrinogen on a first solid support,

b) immobilizing fibrin or a fibrin–derived protein on a second solid support,

c) contacting a library of potential fibrinogen and fibrin binding phage with said first solid support to bind any fibrinogen binding phage in said library,

d) removing the unbound portion of the phage library from said first solid support to obtain a depleted phage library,

e) contacting the depleted phage library with said second support, and

f) removing unbound phage from the second support.

17. A method of detecting fibrin in an animal or human subject comprising the steps of:

detectably labeling a polypeptide according to any one of Claims 1 – 9;

administering to said subject the labeled polypeptide and, thereafter,

detecting the labeled polypeptide in the subject.

18. A method according to Claim 17 wherein said label is radioactive or paramagnetic.

19. A method according to Claim 18 wherein said label is $^{111}In$ or $^{99m}Tc$.

20. A method of according to Claim 17, wherein said detecting step is indicative of deep-vein thrombosis, pulmonary embolism, cardiogenic thrombosis, atherosclerosis or stroke.

21. A method of treating a disease involving thrombus formation, comprising the steps of: administering to an animal or human subject in need of treatment for such a disease a composition comprising a polypeptide according to any one of Claims 1 – 9 conjugated with a thrombolytic agent.

22. The method according to Claim 21 wherein said disease is deep-vein thrombosis, pulmonary embolism, cardiogenic thrombosis, atherosclerosis, myocardial infarct, reperfusion ischemia, or stroke.

23. The method according to Claim 21 wherein said thrombolytic agent is tPA, streptokinase, or urokinase.

24. A recombinant bacteriophage expressing exogenous DNA encoding a fibrin binding polypeptide having an amino acid sequence comprising:
$X_1$–$X_2$–Cys–$X_4$–$X_5$–Tyr–$X_7$–$X_8$–Cys–$X_{10}$–$X_{11}$ (SEQ ID NO:1), wherein
$X_1$ is Arg, Asp, His, Leu, or Phe;
$X_2$ is Ala, Asp, Gly, Pro, or Ser;
$X_4$ is Ala, Glu, Phe, Gly, Ile, Lys, Leu, Met, Arg, Thr, Val, Tyr, Asn, Asp, Gln, His, Ser, or Trp;
$X_5$ is Ala, Tyr, Phe, or Ser;
$X_7$ is Gly, Ala, or DAla;
$X_8$ is Thr, Val, or Ser;
$X_{10}$ is His, Leu, or Phe;
$X_{11}$ is Arg, Asp, or His,
and wherein said fibrin binding polypeptide is displayed on the surface of said bacteriophage.

25. A recombinant bacteriophage expressing exogenous DNA encoding a fibrin binding polypeptide having an amino acid sequence selected from the group consisting of:
Arg–Ser–Cys–Asn–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:5);
His–Asp–Cys–Gln–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:6);
Phe–Ala–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:7);
Arg–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Phe–Asp (SEQ ID NO:8);
Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO:9);
Phe–Ser–Cys–Trp–Tyr–Ser–Leu–His–Cys–His–Arg (SEQ ID NO:10);
Asp–Pro–Cys–Ser–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:11);
Leu–Pro–Cys–Ser–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:12);
Leu–Ser–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Arg (SEQ ID NO:13);
Leu–Ala–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:14);
Asp–Gly–Cys–His–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:15);
Arg–Pro–Cys–Asn–Tyr–Tyr–Gly–Thr–Cys–Leu–His (SEQ ID NO:16); and
wherein said binding peptide is displayed on the surface of said bacteriophage.

26. A magnetic resonance imaging contrast agent comprising a polypeptide fibrin binding moiety comprising the amino acid sequence Tyr–Tyr–Gly–Xaa, wherein Xaa is selected from Thr, Ser or Val, said fibrin binding moiety being coupled to at least one chelator capable of complexing a paramagnetic metal.

27. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 2.

28. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 4.

29. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 5.

30. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 7.

31. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 8.

32. A magnetic resonance imaging contrast agent comprising at least one paramagnetic metal atom and at least one polypeptide according to Claim 9.

33. A magnetic resonance imaging contrast agent according to any one of Claims 26 – 32, wherein said magnetic resonance imaging contrast agent specifically binds fibrin but not fibrinogen.

34. A magnetic resonance imaging contrast agent according to any one of Claims 27 – 32, wherein said magnetic resonance imaging contrast agent further comprises at least one chelator selected from the group consisting of DTPA, DOTA, EDTA, TETA, EHPG, HBED, NOTA, DOTMA, TETMA, PDTA, TTHA, LICAM, and MECAM.

35. A magnetic resonance imaging contrast agent according to Claim 34, wherein said chelator comprises diethylenetriamine or tetraazacyclododecane or a carboxymethyl-substituted derivative thereof.

36. A magnetic resonance imaging contrast agent according to any one of Claims 26 – 32, wherein said paramagnetic metal atom is selected from the group consisting of: $Mn^{2+}$, $Cu^{2+}$, $Fe^{2+}$, $Co^{2+}$, $Ni^{2+}$, $Gd^{3+}$, $Eu^{3+}$, $Dy^{3+}$, $Pr^{3+}$, $Cr^{3+}$, $Co^{3+}$, $Fe^{3+}$, $Ti^{3+}$, $Tb^{3+}$, $Nd^{3+}$, $Sm^{3+}$, $Ho^{3+}$, $Er^{3+}$, $Pa^{4+}$, and $Eu^{2+}$.

37. A magnetic resonance imaging contrast agent according to Claim 36, wherein said multivalent cation is $Gd^{3+}$.

38. A magnetic resonance imaging contrast agent according to Claim 32, selected from the group consisting of: Gd–DTPA–Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO: 67), Gd–DTPA–Gly–Trp–Phe–His–Cys–Pro–Tyr–Asp–Leu–Cys–His–Ile–Leu (SEQ ID NO: 68), Gd–DTPA–Gly–Gln–Trp–Glu–Cys–Pro–Tyr–Gly–Leu–Cys–Trp–Ile–Gln (SEQ ID NO: 69), and Gd–DTPA–Gly–Leu–Pro–Cys–Asp–Tyr–Tyr–Gly–Thr–Cys–Leu–Asp (SEQ ID NO:70).

39. A method for identifying fibrin binding compounds comprising the steps of utilizing a fibrin binding polypeptide according to any one of Claims 1 – 9 to form a complex with fibrin or a fibrin–derived polypeptide, contacting said complex with one or more potential fibrin binding compounds, and determining whether said one or more potential fibrin binding compounds competes with said fibrin binding polypeptide to form a complex with said fibrin or fibrin–derived polypeptide.

40. A diagnostic imaging contrast agent comprising a polypeptide according to any one of Claims 1 – 9.

41. A method of medical imaging comprising the steps of administering to an animal or human subject a pharmaceutical preparation of a contrast agent comprising at least one polypeptide according to any one of Claims 1 – 9 and imaging said contrast agent by a step selected from the group consisting of magnetic resonance imaging, ultrasound imaging, optical imaging, sonoluminescence imaging, photoacoustic imaging, and nuclear imaging.

42. A method of medical imaging according to Claim 41, wherein said administering step is selected from among the group consisting of:
inhaling, transdermal absorbing, intramuscular injecting, subcutaneous injecting, intravenous injecting, and intra–arterial injecting.

43. A method of medical imaging according to Claim 41, wherein said pharmaceutical preparation is packaged in a member selected from among the group consisting of: kit, syringe, vial, bottle, flexible container, packet, or inhaler.

44. A method of medical imaging according to Claim 41, wherein said pharmaceutical preparation is selected from among the group consisting of:
tablet, pill, caplet, suppository, liquid, elixir, aqueous solution, or aqueous suspension.

45. An isolated polypeptide comprising the amino acid sequence
$X_n$–$X_n$–Cys–$X_n$–$X_n$–Tyr–$X_n$–$X_y$–Cys–$X_n$–$X_n$ (SEQ ID NO: 71), wherein
$X_n$ is any amino acid ,
$X_y$ is Thr, Ser, or Val, and
wherein said polypeptide has a greater affinity for fibrin than fibrinogen.

46. An isolated polypeptide comprising the amino acid sequence
Cys–$X_n$–$X_n$–Tyr–$X_n$–$X_y$–Cys (SEQ ID NO: 72), wherein
$X_n$ is any amino acid;
$X_y$ is Thr, Ser, or Val; and
said polypeptide has a greater affinity for fibrin than fibrinogen.

47. A diagnostic imaging contrast agent comprising at least one polypeptide according to Claim 10 and further comprising at least one atom selected from the group consisting of radioactive atoms and paramagnetic atoms.

48. A method of purifying fibrin or fibrin-like polypeptide from a solution containing it comprising contacting the solution with at least one polypeptide according to any one of Claims 1-9, and then separating said polypeptide from said solution.